REMARKS

Claims 1-40 have been cancelled without prejudice. Claims 41-45 have been added. Claims 41-45 are pending.

Support for new claims 41-45 can be found in the specification at, *inter alia*, page 5 (structure of stigmasterol), page 6, line 26 (EPA and DHA), and original claims 5-7. Applicant would also like to direct the Examiner to the Example at page 12 of the specification. The Example, which is one aspect of the invention, provides a detailed synthetic procedure for producing a mixture of stigmasterol esters of EPA and DHA as recited in new claims 41-45.

No new matter has been added by the new claims; therefore, applicants respectfully request that examination continue on the new claims.

A clean copy of all of the pending claims as they are believed to have been cancelled and added is attached to this Amendment as an appendix. The appended clean copy of all of the pending claims is provided only as a convenience to the Examiner and is not intended to be an amendment of the claims pursuant to 37 C.F.R. § 1.121.

I. Rejections under 35 U.S.C. § 102

The Office Action has rejected claims 1, 5, 6, and 34 under 35 U.S.C. § 102(b) over U.S. Patent No. 5,604,216 to Horrobin.

Claims 1, 5, 6, and 34 have been cancelled; however, for the sake of argument, new claims 41-45 will be addressed in view of Horrobin. Although Horrobin discloses cholesterol esters of DHA and EPA, there is no disclosure in Horrobin to use stigmasterol to produce sterol esters of DHA and EPA as recited in new claims 41-45. In the absence of any disclosure of the use of stigmasterol in Horrobin, the present invention is novel.

The Office Action has rejected claims 1, 5, 6, 8, 11, 34, and 40 under 35 U.S.C. § 102(e) over U.S. Patent No. 6,147,236 to Higgins III.

Claims 1, 5, 6, 8, 11, 34, and 40 have been cancelled; therefore, the rejection is moot. Further, applicants assert that Higgins III is not prior art to the claimed invention as recited in

new claims 41-45 because the invention was conceived and reduced to practice prior to (1) the filing date of Higgins III (December 15, 1998) and (2) the priority date of Higgins III (August 25, 1998). Specifically, applicants provide herewith as Exhibit A, the Declaration under 37 C.F.R. § 1.131 of Jeffrey L.C. Wright, whereby he declares that prior to August 25, 1998 and after December 7, 1993, he conceived and reduced the claimed invention to practice in Canada. Enclosed in Exhibit 1 of the Declaration is a notebook page that provides a detailed synthetic procedure for producing stigmasterol esters of DHA and EPA. The source of DHA and EPA is in the material identified as "EPAX" in Exhibit 1. EPAX is also used as the source of DHA and EPA in the Example at page 12 of the present specification. In the procedure enclosed in Exhibit 1, EPAX (135.8 mg) and stigmasterol (108.8 mg) were stirred and placed in a heating element for two hours at 115-119°C. To this mixture, approximately 1 mg of sodium ethoxide (base catalysts) was added. After one hour, another 10 mg of sodium ethoxide was added.

The evidence set forth in the present Declaration demonstrates that the claimed invention was conceived and reduced to practice prior to the priority date and filing date of Higgins III. Thus, Higgins III is not available as prior art in a rejection of the claims of the present invention under 35 U.S.C. § 102(e).

II. Rejections under 35 U.S.C. § 103

The Office Action has rejected claims 5-11, 34, 39, and 40 under 35 U.S.C. § 103 over U.S. Patent No. 6,147,236 to Higgins III in view of Higashidate *et al.* As discussed above, the evidence set forth in the Declaration demonstrates that the claimed invention was conceived and reduced to practice prior to the priority date and filing date of Higgins III. Thus, Higgins III is not available as prior art in a rejection of the claims of the present invention under 35 U.S.C. § 103(a). Therefore, applicants believe this rejection has been rendered moot and respectfully request its withdrawal.

The Office Action has rejected claims 1, 5-11, 34, and 39 under 35 U.S.C. § 103 over U.S. Patent No. 4,588,717 to Mitchell. As mentioned above, claims 1, 5-11, 34, and 39 have been cancelled; however, new claims will be addressed in view of Mitchell.

Mitchell discloses phytosterol esters to be used in vitamin supplements. In particular, Mitchell directs one of ordinary skill in the art to produce phytosterol esters of linoleic acid, linolenic acid, and arachidonic acid. Mitchell, however, is silent with respect to the use of EPA and DHA, which are recited in new claims 41-45. When read in the absence of any other art, one of ordinary skill in the art would not have been motivated to use DHA and EPA.

With respect to claims 1, 5-11, 34, and 39, the Office Action asserts that it would have been obvious to one of ordinary skill in the art to prepare additional beneficial nutritional supplements. The Office Action further states that "there has been ample motivation provided by the art to prepare the instant invention." The Office Action relies upon the disclosure of Higgins III to suggest that DHA and EPA can be esterified with the sterols disclosed in Mitchell to produce the instant invention. First, as described above, there is no motivation in Mitchell to produce sterol esters of DHA or EPA, particularly stigmasterol esters of DHA and EPA. Although it may be known in the art to use DHA or EPA as a health supplement, in the absence of any teaching or suggestion in Mitchell to esterify DHA or EPA, the present invention as recited in new claims 41-45 would not have been obvious. It would require impermissible hindsight to incorporate DHA or EPA into the teachings of Mitchell to produce the sterol esters of the present invention. Finally, for the sake of completeness, Higgins III is not prior art to the present invention.

Assuming, *arguendo*, it would have been obvious to esterify DHA and EPA based on the teachings of Mitchell, the present invention as recited in new claims 41-45 provides superior and unexpected results when compared to the phytosterol esters of linoleic acid, linolenic acid, and arachidonic acid disclosed in Mitchell. The sterol esters recited in new claims 41-45 can reduce cholesterol and triglyceride levels. Evidence of this was previously submitted in the Declarations of Dr. H. Stephen Ewart filed on April 2, 2001 and July 15, 2002. In the Declaration of March 27, 2001 (Exhibit B), data was presented indicating that the sterols esters of the present invention can reduce serum cholesterol and triglyceride levels in animals. In the Declaration of July 10, 2002 (Exhibit C), Dr. Ewart describes that the balance of scientific evidence suggests that omega-3 fatty acids increase cholesterol levels. Indeed, the mechanisms

by which phytoseterols reduce cholesterol and omega-3 fatty acids reduce triglyceride levels are in competition with one another. (*See* ¶ 8-13 of Exhibit C). This is not the case with the present invention, where the esterification of EPA and DHA results in a compound that decreases both serum cholesterol and triglyceride levels in a subject. This is not the case with the stigmasterol esters of linoleic acid, linolenic acid, and arachidonic acid disclosed in Mitchell. Indeed, at best, the stigmasterol esters of linoleic acid, linolenic acid, and arachidonic acid disclosed in Mitchell can only reduce cholesterol levels. Thus, in order to reduce cholesterols and triglyceride levels based on the disclosure of Mitchell, one of ordinary skill in the art would have to use a second component useful in reducing triglyceride levels in combination with the sterol esters of Mitchell (e.g., a blend of fish oil fatty acids and sterol rapeseed fatty acid esters). The present invention avoids this, which ultimately reduces formulation costs.

The Office Action has rejected claims 5-11, 34, and 39 under 35 U.S.C. § 103 over U.S. Patent No. 5,604,216 to Horrobin and U.S. Patent No. 5,502,045 to Miettinen.

Claims 5-11, 34, and 39 have been cancelled; however, for the sake of argument, new claims 41-45 will be addressed in view of Horrobin and Miettinen. As discussed above, there is no disclosure in Horrobin to use stigmasterol to produce sterol esters of DHA and EPA as recited in new claims 41-45. Horrobin only directs one of ordinary skill in the art to esterify fatty acids with cholesterol and not stigmasterol. Similarly, Miettinen only directs the skilled artisan to use sitostanols to produce fatty acid esters, which also do not encompass stigmasterol. Further, Miettinen only directs one of ordinary skill in the art to esterify rapeseed, which does not contain DHA and EPA. Because both Horrobin and Miettinen direct one of ordinary skill in the art to use sterols other than stigmasterol, the invention as recited in new claims 41-45 would not have been obvious to one of ordinary skill in the art.

Further, one of ordinary skill in the art would not have been motivated to substitute cholesterol used in Horrobin for other sterols, particularly stigmasterol, to esterify fatty acids. As discussed above, the compounds of the present invention can reduce cholesterol and triglyceride levels in a subject. Horrobin is not concerned with reducing cholesterol levels in a subject. Indeed, Horrobin teaches the skilled artisan that cholesteryl esters are stable and

resistant to oxidation (column 3, lines 1 and 2). Horrobin further teaches that the increased stability of cholesteryl esters is useful in the preparation of topical creams and ointments (column 3, lines 5-29). Thus, Horrobin does not direct one of ordinary skill in the art to use other phytosterols, particularly stigmasterol, to produce stigmasterol esters of DHA and EPA for reducing cholesterol and triglyceride levels.

Moreover, the present invention as recited in claims 41-45 possesses surprising and unexpected results when compared to the sitostanol esters of rapeseed disclosed in Miettinen. As discussed above, the compounds recited in claims 41-45 can reduce cholesterol and triglyceride levels in a subject. Conversely, the sitstanol esters disclosed Miettinen only reduce cholesterol levels. Enclosed in Exhibit D is a journal article co-authored by Miettinen. In the article, it is disclosed that sitstanol esters of rapeseed oil do not change triglyceride levels. (*See* page 1538, second paragraph in the left column). Thus, the compounds covered in the present invention also have the added benefit of reducing both cholesterol and triglyceride levels in a subject, which was not appreciated at the time the application was filed.

III. Rejections under 35 U.S.C. § 112

The Office Action has rejected claims 1, 5-11, 34, 39, and 40 under 35 U.S.C. § 112, first paragraph, because "the specification, while being enabling for the physterol ester preparation with omega-3 fatty acids selected from DHA, EPA, and SA [, the application] does not reasonably provide enablement for the nutritional supplement for lowering cholesterol and glyceride levels in the bloodstream in a subject."

Claims 1, 5-11, 34, 39, and 40 have been cancelled. Further, new claim 41, which is directed toward stigmasterol esters of DHA, EPA, and/or SA, satisfy the enablement requirements under 35 U.S.C. § 112, first paragraph. As acknowledged by the Office Action, the present specification provides enablement for preparing phytosterol esters of DHA, EPA, and SA. Indeed, one of ordinary skill in the art need only refer to the Example at page 12 of the specification. Thus, the invention as recited in new claims 41-45 is enabled to one of ordinary skill in the art.

The Office Action has rejected claim 1 under 35 U.S.C. § 112, second paragraph. The Office Action states that there are no method steps, particularly steps for lowering of cholesterol and triglyceride in the bloodstream of a subject. Claims 1, 5-11, 34, 39, and 40 have been cancelled; therefore, the rejection is moot. Further, for the sake of clarification, new claims 41-45 are composition claims. Therefore, new claims 41-45 satisfy the requirements of 35 U.S.C. § 112, second paragraph.

IV. Obviousness-Type Double Patenting Rejections

The Office Action asserts that claims 1, 5-11, 34, 39, and 40 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-13 of copending application no. 10/070,181. Applicants await to file a Terminal Disclaimer until all other outstanding rejections are overcome.

CONCLUSION

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

Enclosed is Credit Card Form PTO-2038 in the amount of $1,200.00. No further fee is believed to be due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Lawrence A. Villanueva, J.D., Ph.D. — Date: 3/30/05

APPENDIX

Clean Copy of All Pending Claims after Amendment (for the Examiner's convenience only)

What is claimed is:

41. (New) A composition comprising a sterol ester of an omega-3 fatty acid, wherein the omega-3 fatty acid comprises eicosapentaenoic acid 20:5ω3 (EPA), docosahexaenoic acid 22:6ω3 (DHA) or stearidonic acid 18:4ω3 (SA), and the sterol comprises stigmasterol.

42. (New) The composition of claim 41, wherein the omega-3 fatty acid is eicosapentaenoic acid 20:5ω3 (EPA).

43. (New) The composition of claim 41, wherein the omega-3 fatty acid is docosahexaenoic acid 22:6ω3 (DHA).

44. (New) The composition of claim 41, wherein the omega-3 fatty acid is stearidonic acid 18:4ω3 (SA).

45. (New) The composition of claim 41, wherein the omega-3 fatty acid comprises a mixture of eicosapentaenoic acid 20:5ω3 (EPA) and docosahexaenoic acid 22:6ω3 (DHA), and the sterol comprises stigmasterol.

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